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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,299	GUNJI ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *14-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attachment*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-27 are pending in the application.

Lack of Unity

[2] Applicants' election with traverse of the invention of Group I, claims 1-13 and 26-27, filed January 14, 2004, is acknowledged. Applicants traverse the lack of unity requirement by arguing that the groups of inventions have a common technical feature that represents a contribution over the prior art and assert that all the claims contain the feature of a *Methylophilus* bacterium having increased activities of certain enzymes, which results in the alleged unexpected increase in amino acid producing ability and that the groups should therefore be re-joined and co-examined. Applicants' argument is not found persuasive.

It is noted that applicants' asserted special technical feature linking the inventions of Groups I-VII, *i.e.,* the feature of a *Methylophilus* bacterium having increased activities of certain enzymes, which results in the alleged unexpected increase in amino acid producing ability, is not a shared or corresponding special technical feature present in all claims – particularly those claims of Group I. For example, claim 1 is drawn to a *Methylophilus* bacterium having L-amino acid-producing ability. Nowhere does the claim recite increased activities of certain enzymes, as asserted by applicants. As stated in a previous Office action, Windass et al. (*Nature* 287:396-401) teach a *Methylophilus* bacterium having L-amino acid-producing ability, which is undisputed by applicants.

Therefore, the special technical feature of Group I, *i.e.,* a *Methylophilus* bacterium having L-amino acid-producing ability, is not a contribution over the prior art. As such, the examiner properly applied a lack of unity requirement.

[3] The requirement is still deemed proper and is therefore made FINAL.

[4] Claims 14-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Information Disclosure Statement

[5] All references cited by applicants in the information disclosure statements (IDSs) filed January 10, 2002, October 21, 2002, May 15, 2003, and September 05, 2003 have been considered by the examiner. A copy of each IDS is attached to the instant Office action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[6] Claims 1-8, 10-11, and 26-27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims drawn to a *Methylophilus* bacterium. The claims read on a product of nature and should be amended to indicate the hand of the inventor, *e.g.*, by insertion of "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[7] Claim(s) 4-10 and 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-10 and 26-27 are indefinite in the recitation of "enhanced". The term "enhanced" is unclear absent a statement defining to what the enzyme activity is being compared. The term "enhanced" is a relative term and the claim should define and clearly state as to what the enzyme activity is being compared, *e.g.,* by insertion of the phrase "as compared to a wild-type *Methylophilus* bacterium".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[8] Claims 1-13 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

The claims are drawn to a genus of *Methylophilus* bacteria having L-amino acid producing ability. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only the following representative species of the claimed genus of *Methylophilus* bacteria: 1) wild-type *M. methylotrophus* strain AS1; 2) *M. methylotrophus* strain AR-166 (a *M. methylotrophus* bacterium transformed with expression vectors encoding SEQ ID NO:4 (*Escherichia coli* aspartokinase III) having threonine at position 352 replaced with isoleucine and encoding SEQ ID NO:2 (*Escherichia coli* dihydrodipicolinate synthase) having histidine at position 118 replaced with tyrosine; see pages 48-50 of the specification); 3) *M. methylotrophus* strain AS1/pVIC40 (a *M. methylotrophus* bacterium

transformed with an expression vector encoding a naturally occurring *Escherichia coli* threonine operon; see pages 50-51 of the specification); 4) *M. methylotrophus* strain C138 (a *M. methylotrophus* bacterium transformed with an expression vector encoding a naturally occurring *Escherichia coli* threonine operon; see pages 52-53 of the specification); 5) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* aspartokinase of SEQ ID NO:6; 6) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* aspartic acid semialdehyde dehydrogenase of SEQ ID NO:8 ; 7) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* dihydrodipicolinate synthase of SEQ ID NO:10; 8) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* dihydrodipicolinate reductase of SEQ ID NO:12; and 9) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* diaminopimelate decarboxylase of SEQ ID NO:14. In the instant case, the genus of claimed or recited *Methylophilus* bacteria encompasses species that are WIDELY variant in their physiological, metabolic, and physical characteristics. As such, the disclosure of the disclosed representative species as stated above is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed or recited genus of *Methylophilus* bacteria. Given the lack of description of a representative number of species of the claimed or recited genus of *Methylophilus* bacteria, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[9] Claim(s) 1-13 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a wild-type *Methylophilus methylotrophus* strain AS1 optionally transformed with vectors containing one or more of the following nucleic acids: a nucleic acid encoding SEQ ID NO:4 (*Escherichia coli* aspartokinase III) having threonine at position 352 replaced with isoleucine; a nucleic acid encoding SEQ ID NO:2 (*E. coli* dihydrodipicolinate synthase) having histidine at position 118 replaced with tyrosine; a naturally occurring wild-type *E. coli* threonine synthase operon; a nucleic acid encoding a naturally occurring wild-type *E. coli* dihydrodipicolinate reductase; a nucleic acid encoding the *M. methylotrophus* aspartokinase of SEQ ID NO:6; a nucleic acid encoding the *M. methylotrophus* aspartic acid semialdehyde dehydrogenase of SEQ ID NO:8; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate synthase of SEQ ID NO:10; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate reductase of SEQ ID NO:12; a nucleic acid encoding the *M. methylotrophus* diaminopimelate decarboxylase of SEQ ID NO:14, does not reasonably provide enablement for all *Methylophilus* bacteria with L-amino acid-producing ability and optionally having resistance to an L-amino acid analogue, resistance to L-amino acid auxotrophy, or enhanced L-amino acid biosynthetic enzyme activity as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to

be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass all *Methylophilus* bacteria with L-amino acid-producing ability and optionally having resistance to an L-amino acid analogue, resistance to L-amino acid auxotrophy, or enhanced L-amino acid biosynthetic enzyme activity. The broad scope of claimed or recited *Methylophilus* bacteria is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of *Methylophilus* bacteria broadly encompassed by the claims. In this case the disclosure is limited to a wild-type *M. methylotrophus* strain AS1 optionally transformed with vectors containing one or more of the following nucleic acids: a nucleic acid encoding SEQ ID NO:4 (*Escherichia coli* aspartokinase III) having threonine at position 352 replaced with isoleucine; a nucleic acid encoding SEQ ID NO:2 (*E. coli* dihydrodipicolinate synthase) having histidine at position 118 replaced with tyrosine; a naturally occurring wild-type *E. coli* threonine synthase operon; a nucleic acid encoding a naturally occurring wild-type *E.*

coli dihydrodipicolinate reductase; a nucleic acid encoding the *M. methylotrophus* aspartokinase of SEQ ID NO:6; a nucleic acid encoding the *M. methylotrophus* aspartic acid semialdehyde dehydrogenase of SEQ ID NO:8; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate synthase of SEQ ID NO:10; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate reductase of SEQ ID NO:12; a nucleic acid encoding the *M. methylotrophus* diaminopimelate decarboxylase of SEQ ID NO:14.

- The lack of guidance and working examples: The specification provides only nine working example of the claimed or recited *Methylophilus* bacteria as follows: 1) a wild-type *M. methylotrophus* strain AS1; 2) *M. methylotrophus* strain AR-166 (a *M. methylotrophus* bacterium transformed with expression vectors encoding SEQ ID NO:4 (*Escherichia coli* aspartokinase III) having threonine at position 352 replaced with isoleucine and encoding SEQ ID NO:2 (*Escherichia coli* dihydrodipicolinate synthase) having histidine at position 118 replaced with tyrosine; see pages 48-50 of the specification); 3) *M. methylotrophus* strain AS1/pVIC40 (a *M. methylotrophus* bacterium transformed with an expression vector encoding a naturally occurring *Escherichia coli* threonine operon; see pages 50-51 of the specification); 4) *M. methylotrophus* strain C138 (a *M. methylotrophus* bacterium transformed with an expression vector encoding a naturally occurring *Escherichia coli* threonine operon; see pages 52-53 of the specification); 5) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* aspartokinase of SEQ ID NO:6; 6) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* aspartic acid semialdehyde dehydrogenase of SEQ ID NO:8 ; 7) *M. methylotrophus* transformed with an expression

vector encoding the *M. methylotrophus* dihydrodipicolinate synthase of SEQ ID NO:10; 8) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* dihydrodipicolinate reductase of SEQ ID NO:12; and 9) *M. methylotrophus* transformed with an expression vector encoding the *M. methylotrophus* diaminopimelate decarboxylase of SEQ ID NO:14. These working examples fail to provide the necessary guidance for making the entire scope of claimed or recited *Methylophilus* bacteria. Other than transforming a *M. methylotrophus* bacterium with an expression vector containing one or more of the following nucleic acids: a nucleic acid encoding SEQ ID NO:4 (*Escherichia coli* aspartokinase III) having threonine at position 352 replaced with isoleucine; a nucleic acid encoding SEQ ID NO:2 (*E. coli* dihydrodipicolinate synthase) having histidine at position 118 replaced with tyrosine; a naturally occurring wild-type *E. coli* threonine synthase operon; a nucleic acid encoding a naturally occurring wild-type *E. coli* dihydrodipicolinate reductase; a nucleic acid encoding the *M. methylotrophus* aspartokinase of SEQ ID NO:6; a nucleic acid encoding the *M. methylotrophus* aspartic acid semialdehyde dehydrogenase of SEQ ID NO:8; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate synthase of SEQ ID NO:10; a nucleic acid encoding the *M. methylotrophus* dihydrodipicolinate reductase of SEQ ID NO:12; a nucleic acid encoding the *M. methylotrophus* diaminopimelate decarboxylase of SEQ ID NO:14, the specification provides no further guidance as to altering a *Methylophilus* bacterium.

- The high degree of unpredictability in the art: There is a high degree of unpredictability for altering bacteria with an expectation of obtaining a bacterium having

the desired characteristics – particularly in view of the infinite number of modifications of a *Methylophilus* bacterium that are encompassed by the claims that result in the desired *Methylophilus* bacterium. Such modifications include those resulting from non-specific methods of altering a cell, *e.g.,* chemical and UV mutagenesis and chromosomal DNA shuffling. Using these methods, a skilled artisan would recognize the high degree of unpredictability in obtaining the desired *Methylophilus* bacterium.

- The amount of experimentation required is undue: While methods of modifying the L-amino acid producing ability of a given bacteria, *e.g.*, by transformation of the bacteria with a plasmid for overexpression of a desired enzyme, it is not routine in the art to screen for *all* bacteria having an infinite number of modifications and further having the desired characteristics, as encompassed by the instant claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[10] Claim(s) 1-3 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (*Appl Microbiol Biotechnol* 48:105-108; cited by applicants in the IDS filed May 15, 2003). The claims are drawn to a *Methylophilus* bacterium having L-amino acid-producing ability and optionally wherein the L-amino acid is limited to those recited in claim 2, wherein the bacterium shows amino acid auxotrophy, or wherein the bacterium is limited to *M. methylotrophus.* Kim et al. teach a *M. methylotrophus* having auxotrophy to serine and alanine (page 107, Table 1). While Kim et al. do not specifically teach that the serine/alanine auxotrophic *M. methylotrophus* has the ability to produce L-amino acids, this is an inherent characteristic of the bacterium. This anticipates claims 1-3 and 11 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[11] Claim(s) 1-9, 11-13, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kojima et al. (US Patent 6,040,160) in view of Barth et al. (EP 0037273; cited by applicants in the IDS filed January 10, 2002), De Maeyer et al. (*PNAS* 79:4256-4259), and Kim et al. The claims are drawn to a *Methylophilus* bacterium having L-amino acid producing ability and a method for producing an amino acid using said *Methylophilus* bacterium.

Kojima et al. teach isolation of a nucleic acid encoding an *E. coli* aspartokinase III having threonine at position 352 replaced with isoleucine (Example 2) and a nucleic acid encoding an *E. coli* dihydrodipicolinate synthase having histidine at position 118 replaced with tyrosine (Example 1). Kojima et al. teach transformation of *E. coli* with an expression vector encoding the mutant aspartokinase III resulted in feedback resistance of the transformant to L-lysine and AEC, an L-lysine analogue (columns 22-23) and transformation of *E. coli* with an expression vector encoding the mutant dihydrodipicolinate synthase resulted in feedback resistance of the transformant to AEC (column 19). Kojima et al. teach a method for producing L-lysine by co-expressing the nucleic acids encoding the mutant aspartokinase III and dihydrodipicolinate synthase enzymes, which consequently resulted in a marked increase in L-lysine production (columns 29-30). Kojima et al. teach that co-expression of nucleic acids encoding the mutant aspartokinase III and dihydrodipicolinate synthase enzymes with additional co-

expression of a nucleic acid encoding wild-type *E. coli* dihydrodipicolinate reductase (see column 34 for method of isolation) resulted in an increase in L-lysine production as compared to co-expression of nucleic acids encoding the mutant aspartokinase III and dihydrodipicolinate synthase enzymes alone (column 35, Table 12). Kojima et al. do not teach substituting *M. methylotrophus* for *E. coli* as an expression host.

Kim et al. disclose the teachings as described above. Additionally, Kim et al. teach methylotrophic bacteria have been extensively studied and have potential commercial value for producing amino acids and provide a specific example of a methylotrophic bacteria as *M. methylotrophus* (page 105, left column, bottom).

Barth et al. teach that most genetic manipulation of microorganisms has involved *E. coli*, which is found in man and there are advantages to using an organism that is not normally found in man and which is less likely to infect him (page 1, middle). Barth et al. teach that a preferred microorganism is *M. methylotrophus,* which can be grown rapidly and efficiently, does not infect man, and is particularly safe for large scale biosynthesis (page 5, bottom). Barth et al. teach construction of expression vectors encoding a murine dihydrofolate reductase (DHFR) and transformation of *E. coli* and *M. methylotrophus* with the resulting expression vectors (pages 8-10). The transformants were cultured (the *M. methylotrophus* transformant was cultured in the presence of methanol as the carbon source – see page 10) and the cell extracts analyzed for DHFR activity (pages 10-11). The cell extract of the *M. methylotrophus* transformants showed a significantly higher DHFR activity than the *E. coli* transformants (page 11).

De Maeyer et al. teach construction of expression vectors encoding a human alpha1 interferon (page 4257, left column) and transformation of *E. coli* and *M. methylotrophus* with the expression vectors (page 4256, right column). The transformants were cultured (the *M. methylotrophus* transformant was cultured in the presence of methanol as the carbon source – see page 4256, right column) and analyzing the cell extracts for interferon activity (page 4258, Table 4). The cell extract of the *M. methylotrophus* transformants showed an equivalent level of interferon activity as compared with the *E. coli* transformants (page 4258, right column). De Maeyer et al. reiterate those advantages of using *M. methylotrophus* over *E. coli* as an expression host as taught by Barth et al. (page 4259, left column, bottom).

At the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Kojima et al., Barth et al., De Maeyer et al., and Kim et al. to transform *M. methylotrophus* with expression vectors encoding the mutant aspartokinase III and dihydrodipicolinate synthase and wild-type dihydrodipicolinate reductase as taught by Kojima et al. and to use the resulting transformant for producing L-lysine. One would have been motivated to transform *M. methylotrophus* with expression vectors encoding the mutant aspartokinase III and dihydrodipicolinate synthase and wild-type dihydrodipicolinate reductase as taught by Kojima et al. and to use the resulting transformant for producing L-lysine because of the advantages of using *M. methylotrophus* as compared to *E. coli* as taught by Barth et al. and because of the potential commercial value of *M. methylotrophus* for amino acid production as taught by Kim et al. One would have a reasonable expectation of success for

transforming *M. methylotrophus* with expression vectors encoding the mutant *E. coli* aspartokinase III and dihydrodipicolinate synthase and wild-type *E. coli* dihydrodipicolinate reductase as taught by Kojima et al. and to use the resulting transformant for producing L-lysine as Kojima et al. teach the methods of isolating the encoding nucleic acids and Barth et al. and De Maeyer et al. teach the use of *M. methylotrophus* for heterologous protein expression. Therefore, claims 1-9, 11-13, and 26-27, drawn to a *Methylophilus* bacterium and a method of use thereof as described above would have been obvious to one of ordinary skill in the art.

[12] Claim(s) 1-4, 7, and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (US Patent 5,939,307) in view of Barth et al., De Maeyer et al., and Kim et al. The claims are drawn to a *Methylophilus* bacterium having L-amino acid producing ability and a method for producing an amino acid using said *Methylophilus* bacterium.

Wang et al. teach construction of an expression vector encoding an *E. coli* threonine operon encoding aspartokinase, homoserine dehydrogenase, homoserine kinase, and threonine synthase (Figures 1-4 and column 6, bottom) and transformation of *E. coli* with the resulting vector, which led to an increase in the production of L-threonine (Examples 1-3). Wang et al. do not teach substituting *M. methylotrophus* for *E. coli* as an expression host.

Kim et al., Barth et al., and De Maeyer et al. disclose the teachings as described above.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Wang et al., Barth et al., De Maeyer et al., and Kim et al. to transform *M. methylotrophus* with an expression vector encoding an *E. coli* threonine operon and to use the resulting transformant for producing L-threonine. One would have been motivated to transform *M. methylotrophus* with an expression vector encoding an *E. coli* threonine operon and to use the resulting transformant for producing L-threonine because of the advantages of using *M. methylotrophus* as compared to *E. coli* as taught by Barth et al. and because of the potential commercial value of *M. methylotrophus* for amino acid production as taught by Kim et al. One would have a reasonable expectation of success for transforming *M. methylotrophus* with an expression vector encoding an *E. coli* threonine operon and to use the resulting transformant for producing L-threonine as Wang et al. teach the a method of isolating the encoding nucleic acid and Barth et al. and De Maeyer et al. teach the use of *M. methylotrophus* for heterologous protein expression. Therefore, claims 1-4, 7, and 10-13, drawn to a *Methylophilus* bacterium and a method of use thereof as described above would have been obvious to one of ordinary skill in the art.

Double Patenting Rejection(s)

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[13] Claims 1, 3-4, and 11-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of US Patent 6,350,596 ('596 Patent). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-4, and 11-12 are generic to all that is recited in claims 1-8 of the '596 Patent. That is, claims 1-8 of the '596 Patent fall entirely within the scope of claims 1, 3-4, and 11-12 or, in other words, claims 1, 3-4, and 11-12 of the instant application are anticipated by claims 1-8 of the '596 Patent.

Conclusion

[14] Status of the claims:

- Claims 1-27 are pending.
- Claims 14-25 are withdrawn from consideration.

- Claims 1-13 and 26-27 are rejected.

- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

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